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June 3, 2015

Dr. David Haas
President, AAOF
401 N. Lindbergh
St. Louis, MO 63141
Fax: 314-997-1745

Dear Dr. Haas:

Enclosed is the final report for my two AAOF Faculty Development Awards for 1998/1999 and 1999/2000. Previously, I have sent in a final report for my 1995/1996 award.

Principle Investigator: Dr. Andrew C. Lidral
Co-Investigators: Dr. Jeffrey Murray, MD. University of Iowa
Dr. Mary Marazita, PhD. University of Pittsburgh
Dr. Mauricio Arcos-Burgos, MD, PhD. University of Antioquia, Colombia

Title of Project: "Mutation Screen of the TGFB3 Gene in Patients with Nonsyndromic Cleft Lip".

Institution: Ohio State University (currently I am at the University of Iowa)

Project summary:
Cleft lip with or without palate (CL/P) is the fourth most common birth defect and affects 1/750 births. Studies indicate that the CL phenotype has a complex mode of inheritance with the possible involvement of 2-20 genes. Animal research has implicated transforming growth factor beta three (TGFB3) in normal palatogenesis. TGFB3 is a signaling molecule that is expressed on the medial edge epithelium of the developing palate. Transgenic mice in which TGFB3 has been inactivated are born with a cleft palate (CPO) phenotype. Recently, an association between TGFB3 and cleft lip was detected in an Iowan population, but no association was found with CPO in the same Iowan population. The purpose of this study was to further delineate the role of TGFB3 in the etiology of CL/P. A mutation screen was performed for most of the TGFB3 coding region (except exon 4) and the upstream region in 190 CL/P patients from Iowa. No common mutations were identified in the coding region. However, a polymorphism was identified in the upstream region in 5/248 CL/P and 4/152 control chromosomes (p=0.68). In addition, a combination of two variants, one in the upstream region and another between two exons, was found to be associated with cleft lip (p=0.008). It will be necessary to perform functional assays of these variants to determine whether they may have an etiologic role. However, it can be clearly concluded that coding mutations in TGFB3 are not common in cleft lip patients. This suggests that the association may be explained by mutations in the regulatory regions of TGFB3. To further evaluate the role of TGFB3, linkage was tested in 43 Colombian cleft lip families. Linkage between TGFB3 and CL/P was significantly excluded in the Colombian families. **Conclusions**: A polymorphic variant was discovered in the Iowa population that may potentially alter the function of TGFB3. Also, the cause of CL/P is different in the Iowa population as compared to the Colombian population.

In addition, I have had the opportunity to pursue my goals in Orthodontic Education which include patient care, teaching and research. In fact, I am living my dreams that I set out to pursue just under 10 years ago. Much of this has been possible due to the various funding available through the AAOF, which is an invaluable seed grant mechanism to allow me to develop credibility to obtain NIH funding. This has led to a variety of grants being funded including, a March of Dimes Basil O'Connor award which was renewed as a March of Dimes Research Award. In addition, I have received NIH funding in the form of a small grant, a project on the University of Iowa - NIH Comprehensive Oral Health Research Center of Discovery entitled "A Comprehensive Program to Investigate Craniofacial and Dental Anomalies", and a independent investigator initiated NIH grant (R01). I am very pleased to have been a recipient of the AAOF Awards granted to me as they provided invaluable research money to develop preliminary data necessary to obtain these grants and have thus been very important in launching my academic career.

If you have any questions, please do not hesitate to contact me.

Sincerely,

Andrew Lidral DDS, PhD
Associate Professor
Email: Andrew-Lidral@UIowa.edu